

Bibliographic Information

Carbonic acid amides of imidazoles, triazoles, and tetrazoles. Staab, Heinz A. (Badische Anilin- & Soda-Fabrik AG). (1958), DE 1033210 19580703 Patent language unavailable. CAN 54:74703 AN 1960:74703 CAPLUS

Patent Family Information

Patent No.	Kind	Date	Application No.	Date
DE 1033210		19580703	DE 1956-B42718	19561206

Abstract

The title compds. which easily evolved CO₂ and were useful as blowing agents, were made by treating the heterocyclic compds. with COCl₂. Thus, imidazole (I) 3 in anhyd. tetrahydrofuran 125 parts was treated under exclusion of air with COCl₂ (4 moles of amine to 1 mole of COCl₂). Excess COCl₂ was removed with N, the pptd. hydrochloride of I filtered, and the soln. concd. in vacuo to obtain pure N,N'-carbonyldiimidazole, m. 115.5-16°. By the same procedure were prepd. N,N'-carbonylditriazole, m. 136° (theoretical yield), N,N'-carbonyldibenzimidazole, m. 182-3°, and N,N'-carbonyldibenztriazole, m. 183-5° (decompn.).

Patent Classifications

U.S.: 12P.

Indexing -- Section 10G (Organic Chemistry: Heterocyclic Compounds)

Blowing agents
(heterocyclic urea analogs for)

v-Triazole, urea analogs

57-13-6, Urea
(heterocyclic analogs)

83-39-6, Imidazole-4,5-dicarboxamide
530-62-1, Imidazole, 1,1'-carbonyldi-
14667-54-0, Benzimidazole, 1,1'-carbonylbis-
59399-27-8, Imidazole-4,5-dicarboxylic acid, dibutyl ester
66838-71-9, 2,4-Pentadienophenone, 5,5-dichloro-
68985-05-7, 1H-Benzotriazole, 1,1'-carbonylbis-
85387-25-5, 4H-1,2,4-Triazole, 4,4'-carbonylbis-
100862-32-6, Imidazole-4,5-dicarboxylic acid, 2-methyl-, dibutyl ester
107523-91-1, 2,4-Pentadienophenone, 5,5-dichloro-, (2,4-dinitrophenyl)hydrazone
(prepn. of)

288-32-4, Imidazole
27988-97-2, Tetrazole
(urea analogs)

rolidine (b.p. 180°), and 1,2-dicarbethoxy-3-dicarbethoxy-methyl-4-(2-dimethylaminoisopropyl)pyrrolidine (b.p. 170°).

Hiroshi Kataoka

Derivatives of 2-pyrrolidine. Takeda Pharmaceutical Industries, Ltd. (by Suetatsuoka, Kuniyoshi Tanaka, Yoshio Ueno, Masuo Miyamoto, Yasushi Sanno, and Masao Uchibayashi). Japan. 4821(59), June 11. To 1 g. Na in 18 cc. EtOH was added 8.2 g. 1,2-dicarbethoxy-3-acetoxy-4-isopropylpyrrolidine, the mixt. refluxed 2 hrs., 3 cc. AcOH and 10 cc. H₂O added with ice cooling, the mixt. extd. with C₆H₆, the ext. evapd., and distd. *in vacuo* to give 3.2 g. 1,2-dicarbethoxy-4-isopropyl-2-pyrrolidine, b.p. 125-30°.

Hiroshi Kataoka

Pyrrolidine derivatives. Takeda Pharmaceutical Industries, Ltd. (by Suetatsuoka, Kuniyoshi Tanaka, Yoshio Ueno, Mikio Honjo, and Masao Uchibayashi). Japan. 3369(59), May 7. To 1.2 g. Na in 25 cc. EtOH was added 8.8 g. di-Et aminomalonate, 24.4 g. 2-isopropyl-bromopropane dropped in, the mixt. boiled 13 hrs., the EtOH evapd. *in vacuo*, the residue adjusted to pH 2 with 10% HCl, washed with Et₂O, made strongly alk. with 10% NaOH, extd. with Et₂O, and the ext. distd. *in vacuo* to give 2.2 g. 2,2-dicarbethoxy-4-isopropylpyrrolidine, b.p. 103-5°. Similarly were prepd. 2,2-dicarbethoxy-4-(2-ethoxyisopropyl)pyrrolidine (b.p. 145°) and 2,2-dicarbethoxy-4-(2-phenoxyisopropyl)pyrrolidine (b.p. 180-1°).

Hiroshi Kataoka

3-Sulfanilamido-5-methylisoxazole. Shionogi & Co., Ltd. (by Hideo Kano, Kazuko Ogata, Haruo Nishimura, and Kiyoshi Nakajima). Japan. 5566(59), June 29. Et 5-methylisoxazole-3-carbamate (1.7 g.) was heated with 5 cc. 10% NaOH soln. 8 hrs., extd. with Et₂O or C₆H₆, the ext. evapd., and recrystd. from C₆H₆ to give 2-amino-5-methylisoxazole (I), m. 61-2°. To 0.9 g. I in 5 cc. pyridine was added 2.0 g. *p*-acetamidobenzenesulfonyl chloride, the mixt. kept 1 hr., H₂O added, and the ppt. recrystd. from EtOH to give 2.5 g. 3-(*p*-acetamidobenzenesulfonylamido)-5-methylisoxazole (II), m. 220-1°. II (2 g.) was boiled with 10 cc. 10% NaOH soln. 1 hr., cooled, acidified with AcOH, and the ppt. recrystd. from EtOH to give 1.5 g. title product, m. 167°; di-Ac deriv. m. 209-10°. The product inhibited the growth of *Shigella dysenteriae*, *Salmonella paratyphi*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Salmonella typhosa*, *Bacillus subtilis*, and *Mycobacterium tuberculosis*.

Hiroshi Kataoka

***N*-Acetyl derivatives of 5-(*p*-aminophenylsulfonylamido)-3,4-dimethylisoxazole.** Shionogi Co., Inc. (by Hideo Kano). Japan. 4822(59), June 11. 5-(*p*-Aminophenylsulfonylamido)-3,4-dimethylisoxazole (13.4 g.) in 15 cc. pyridine was heated on a steam-bath, stirred with 7 g. Ac₂O at 40-60°, cooled, H₂O added, and isolated mass washed with 5% NaOH and H₂O to give 148 g. title product, flakes, m. 183-4° (MeOH), without bitter taste.

Hiroshi Kataoka

Acyl derivatives of 6-hydroxy-2-aminobenzothiazole. Farbenfabriken Bayer Akt.-Ges. (by Gerhard Schrader). Ger. 927,507, May 9, 1955 (Cl. 12p). *O*-Acyl derivs. of 6-hydroxy-2-aminobenzothiazole (I) were prepd. by treating I with acyl halides or chloroformic acid esters. Thus, 16.5 g. I was dissolved in 100 ml. *N*-NaOH and 14.5 g. BzCl added at 10-15° to ppt. 6-benzoyloxy-2-aminobenzothiazole, m. 178° (acetonitrile). Similarly prepd. were 6-(dimethylcarbamoyloxy)-2-aminobenzothiazole, m. 244°, and 6-methylsulfonyloxy-2-aminobenzothiazole, m. 192°. Chloroformic acid Et ester reacted with I to give 6-(carbethoxyoxy)-2-aminobenzothiazole, m. 244°. I (18.5 g.) was dissolved in MeEtCO, 15 g. CaCO₃ added and then 19 g. *O,O*-diethylthiophosphoric acid chloride to give 21 g. *O,O*-diethylthiophosphoric acid ester of I.

J. J. Bohning

Pyrazole derivatives. Shionogi & Co., Ltd. (by Akira Takamizawa and Sadao Hayashi). Japan. 5568(59), June 29. *p*-Nitrophenylhydrazine (0.3 g.), 0.35 g. α -methoxyethoxymethyl- β -ethoxypropionitrile, and 2 g. concd. HCl were dissolved in 25 cc. EtOH, refluxed 30 min., and concd. to give 0.25 g. 1-(*p*-nitrophenyl)-4-cyanopyrazole (I), m. 190-2° (EtOH-Me₂CO). I (0.3 g.) was dissolved in 300 cc. EtOH, 0.5 cc. concd. HCl and 0.1 g. 2.5% Pd-C added, and the mixt. catalytically reduced to give 0.22 g. 1-(*p*-aminophenyl)-4-cyanopyrazole, plates, m. 174-5° (C₆H₆). Similarly were prepd. 1-phenyl-4-cyanopyrazole (m. 93-4°) and 1-phenylpyrazole-4-carboxylic acid (needles, m. 218-19°). These were useful as analgesics.

Hiroshi Kataoka

Pyrazole derivatives. Shionogi & Co., Ltd. (by Akira

Takamizawa and Sadao Hayashi). Japan. 5674(59), June 30. To 2 g. Et α -diethoxymethyl- β -ethoxypropionate and 1.3 g. *p*-nitrophenylhydrazine in 50 cc. EtOH was dropped a small amt. of concd. HCl with stirring, refluxed 30 min., concd. to 20 cc., and cooled to give 0.8 g. 1-(*p*-nitrophenyl)-4-carbethoxypyrazole, yellow needles, m. 183-4° (EtOH). Similarly was prepd. 1-phenyl-4-carbethoxypyrazole (I), needles, m. 100° (dil. EtOH). I was heated with HCl to give 1-phenyl-4-carboxypyrazole, m. 218-19° (C₆H₆). The compds. were useful as tranquilizers.

Hiroshi Kataoka

Certain esters of 1,2-diaryl-3-hydroxy-4-substituted-pyrazolin-5-ones. Ellis R. Pinson, Jr. (to Chas. Pfizer & Co., Inc.). U.S. 2,905,694, Sept. 22, 1959. These esters were possessed of valuable *analgesic, antipyretic, and anti-inflammatory properties* with reduced toxicity compared with other known derivs. They could be administered orally in the form of tablets or suspensions. To a mixt. of 5 g. 4-butyl-1,2-diphenylpyrazolidine-3,5-dione, 50 ml. CHCl₃, and 6.7 ml. Et₃NH was added 2.48 ml. *o*-toluoyl chloride in 10 ml. CHCl₃ with stirring for 0.5 hr. This mixt. was extd. with dil. aq. HCl, washed with H₂O, and dried. The dry CHCl₃ soln. was evacuated. The residue on trituration with petr. ether yielded 4.75 g. 1,2-diphenyl-3-(*o*-toluoyloxy)-4-butylpyrazolone, m. 95-6°. Similarly prepd. were: 1,2-diphenyl-3-benzoyloxy-4-butylpyrazolone, m. 115-16°; 1,2-diphenyl-3-isobutyroxy-4-butylpyrazolone, m. 120-30°; Et 1,2-diphenyl-4-butylpyrazolonyl-3-carbonate, m. 65.5-7.5°. A tablet base prepn. was given.

Kathryn M. Wolfe

***N*-Alkyl derivatives of diphenylhydantoin.** Dai-Nippon Drug Manuf. Co. (by Shige Toyonshima, Hiroshi Tatsumi, and Masanao Shimizu). Japan. 6114(59), July 14. To 5 g. 5,5-diphenylhydantoin in 40 cc. EtOH was added 7 g. 12% NaOH soln., 4.5 g. AmBr added gradually, the mixt. boiled 15 min., cooled, the EtOH evapd. *in vacuo*, the residue washed with H₂O and petr. ether, and recrystd. from dil. EtOH to give 4.5 g. 5,5-diphenyl-3-amyldantoin, needles, m. 116-18°. Similarly were prepd. 3-isoamyl (needles, m. 145-6°), 3-hexyl (plates, m. 81-3.5°), and 3-lauryl (needles, m. 68-7°) homologs, useful chemotherapeutics for diseases caused by virus.

Hiroshi Kataoka

Arylsulfonyl derivatives of bicyclic guanidines. Monsanto Canada Ltd. (by Arthur F. McKay and Maria E. Krelling). Brit. 826,838, Jan. 20, 1960. See U.S. 2,865,913 (Cl. 53, 8180c).

P. M. B.

Imidazoles. Wm. J. Palaverda and Erwin F. Schoenewaldt (to Merck and Co., Inc.). U.S. 2,905,692, Sept. 22, 1959. Di(lower alkyl) 4,5-imidazoledicarboxylates are produced in good yield by treating a di(lower alkyl) tartrate dinitrate with either a lower aliphatic aldehyde, formaldehyde, or a formaldehyde precursor and NH₃ in a medium of pH 3.5-6.5. For example, 0.0162 g. di-Bu tartrate dinitrate is added dropwise at 15° to 17 ml. MeOH, 17 ml. H₂O, 4 ml. glacial AcOH, 7.1 g. AcONH₄, and 1.77 g. hexamethylenetetramine, the mixt. stirred 15 hrs. at room temp., dild. with an equal vol. of H₂O, and 2.8 g. di-Bu 4,5-imidazoledicarboxylate filtered off in 84.5% yield, m. 107.5-8.5° (aq. MeOH). Similarly prepd. are: 4,5-imidazoledicarboxamide, di-Bu 2-methyl-4,5-imidazoledicarboxylate, and 46% di-Bu 4,5-imidazoledicarboxylate.

Kathryn M. Wolfe

Carbonic acid amides of imidazoles, triazoles, and tetrazoles. Badische Anilin- & Soda Fabrik Akt.-Ges. (by Heinz A. Staab). Ger. 1,033,210, July 3, 1958 (Cl. 12p). The title compds. which easily evolved CO₂ and were useful as *blowing agents*, were made by treating the heterocyclic compds. with COCl₂. Thus, imidazole (I) 3 in anhyd. tetrahydrofuran 125 parts was treated under exclusion of air with COCl₂ (4 moles of amine to 1 mole of COCl₂). Excess COCl₂ was removed with N, the pptd. hydrochloride of I filtered, and the soln. concd. *in vacuo* to obtain pure *N,N'*-carbonyldimidazole, m. 115.5-16°. By the same procedure were prepd. *N,N'*-carbonylditriazole, m. 136° (theoretical yield), *N,N'*-carbonyldibenzimidazole, m. 182-3°, and *N,N'*-carbonyldibenztriazole, m. 183-5° (decompn.).

R. W. Rosner

Synthesis of paracotoin and some α -pyrones. M. Julia and J. Bullot. *Bull. soc. chim. France* 1959, 1849.—RCOMe condensed with Cl₂C:CHCHO (I) in alc. in the presence of Ba(OH)₂ at 0° gave Cl₂C:CHCH:CHCOR (II). In this way, the following II were prepd. (R, m.p., and m.p. of the 2,4-dinitrophenylhydrazones given): Ph, 75-6°, 184°;



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 BEKANNTMACHUNG
 DER ANMELDUNG
 UND AUSGABE DER
 AUSLEGESCHRIFT 3. JULI 1958

1

Es wurde gefunden, daß man Kohlensäureamide von Imidazolen, Triazolen und Tetrazolen mit einem an ein N-Atom gebundenen, reaktionsfähigen Wasserstoffatom in nahezu theoretischer Ausbeute erhält, wenn man diese stickstoffhaltigen heterocyclischen Verbindungen mit Phosgen umsetzt. Die Ausgangsverbindungen werden im allgemeinen in solchen Mengenverhältnissen miteinander umgesetzt, daß 4 Mol der heterocyclischen Verbindung auf 1 Mol Phosgen entfallen. Von den verwendeten 4 Mol der stickstoffhaltigen heterocyclischen Verbindung werden 2 Mol als entsprechendes Hydrochlorid zurückgewonnen.

Zweckmäßig führt man die Reaktion in wasserfreien indifferenten organischen Lösungsmitteln durch. Besonders gut geeignet ist Tetrahydrofuran, doch lassen sich auch andere Äther, die unter den genannten Bedingungen nicht mit Phosgen reagieren, sowie aliphatische oder aromatische Kohlenwasserstoffe verwenden. Es genügt vollständig, bei Raumtemperatur zu arbeiten.

Die erhaltenen Verbindungen spalten unter hydrolysierenden Bedingungen sehr leicht Kohlendioxyd ab und lassen sich deshalb vorteilhaft als Blähmittel verwenden.

Die in den Beispielen genannten Teile sind Gewichtsteile.

Beispiel 1

In eine Lösung von 3 Teilen Imidazol in 125 Teilen wasserfreiem Tetrahydrofuran wird unter Ausschluß von Luftfeuchtigkeit Phosgen im Molverhältnis 4:1 eingeleitet. Ein Überschuß an Phosgen wird durch Einleiten von getrocknetem Stickstoff entfernt. Anschließend saugt man vom ausgefallenen Imidazol Hydrochlorid ab und engt die Tetrahydrofuranlösung im Vakuum ein. Um letzte Reste Imidazolhydrochlorid zu entfernen, kann man den kristallisierten Rückstand einige Male mit je 50 Teilen siedendem Benzol extrahieren. Man erhält reines N,N'-Carbonyl-di-imidazol vom Schmelzpunkt 115,5 bis 116° C.

Beispiel 2

Führt man die Umsetzung, wie im Beispiel 1 beschrieben wurde, mit 2 Teilen 1,2,4-Triazol an Stelle von 3 Teilen Imidazol in 100 Teilen wasserfreiem Tetrahydrofuran durch, so verläuft die Reaktion ana-

 Verfahren zur Herstellung
 von Kohlensäureamiden von Imidazolen,
 Triazolen und Tetrazolen

Anmelder:

 Badische Anilin- & Soda-Fabrik
 Aktiengesellschaft, Ludwigshafen/Rhein

 Dr. Heinz August Staab, Heidelberg,
 ist als Erfinder genannt worden

2

log. Man erhält N,N'-Carbonyl-di-triazol vom Schmelzpunkt 136° C in theoretischer Ausbeute.

Beispiel 3

In eine Lösung von 4,7 Teilen Benzimidazol in 125 Teilen wasserfreiem Tetrahydrofuran wird unter Ausschluß von Luftfeuchtigkeit ein Teil gasförmiges Phosgen im Lauf von 5 Minuten eingeleitet. Man saugt von dem ausgefallenen Benzimidazolhydrochlorid ab. Das Filtrat hinterläßt beim Einengen im Vakuum bei etwa 40° C weiße Kristalle von N,N'-Carbonyl-di-benzimidazol. Beim Umkristallisieren aus wasserfreiem Benzol erhält man farblose Nadeln vom Schmelzpunkt 182 bis 183° C.

Beispiel 4

Wie im Beispiel 3 beschrieben wurde, setzt man 4,75 Teile Benztriazol mit 1 Teil Phosgen um und arbeitet das Reaktionsgemisch in gleicher Weise auf. Beim Umkristallisieren aus wasserfreiem Benzol erhält man das N,N'-Carbonyl-di-benztriazol vom Schmelzpunkt 183 bis 185° C (und Zersetzung) in farblosen Nadeln.

PATENTANSPRUCH:

Verfahren zur Herstellung von Kohlensäureamiden von Imidazolen, Triazolen und Tetrazolen mit einem an ein Stickstoffatom gebundenen, reaktionsfähigen Wasserstoffatom, dadurch gekennzeichnet, daß diese Verbindungen mit Phosgen umgesetzt werden.